

Amendment B
U.S. Appl. 09/942,174
May 11, 2004

Remarks

Claim Amendments

Claims 8-9, 11 and 13 are amended in this Amendment B. Claims 1-7, 12, 14 and 16 are canceled. Upon entry of the amendment, claims 8-11, 13 and 15 will be pending in the application.

Applicants have amended claims 8 and 9 to more particularly define the invention and to improve the form of the claims. No new matter has been added.

Applicants have amended claims 11 and 13 to more particularly define the conditions treated by the methods of the present invention. No new matter has been added. It is respectfully submitted that each of the amended claims is supported in the specification and by canceled claims 12 and 14.

Claims 1-7, 12, 14 and 16 have been cancelled. Applicants reserve the right to pursue any canceled subject matter and/or any other subject matter disclosed in this application in one or more later-filed divisional and/or continuation applications.

Rejection under 35 U.S.C. §112, first paragraph

A. Claims 10, 11, 13 and 15 are enabled.

Applicants respectfully request reconsideration of the rejection of claims 10-16 as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention.

In order to be enabled under 35 U.S.C. §112, first paragraph, "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'." *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Questions of enablement are evaluated against the claimed subject matter and the first analytical step requires a determination of exactly what subject matter is encompassed by the claims. See, MPEP 2164.08. All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further, the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

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In the instant case, the Examiner maintains her rejection on the premise that the claims, which are directed to the treatment of tumor metastasis, tumor growth and solid tumor growth, are not enabled for every type of "tumor." However, Applicants respectfully point out that claim 11 as amended provides a method for treating $\alpha_v\beta_3$ -mediated tumor metastasis, $\alpha_v\beta_3$ -mediated tumor growth and $\alpha_v\beta_3$ -mediated solid tumor growth rather than merely tumor metastasis, tumor growth and solid tumor growth generally. As described at page 1, lines 20 to 32 of the specification, it is well known within the art of oncology that the $\alpha_v\beta_3$ integrin "plays a role in various conditions or disease states including tumor metastasis, solid tumor growth (neoplasia), osteoporosis (Ross et al., *J. Biol. Chem.*, 1987, 262, 7703), Paget's disease, humoral hypercalcemia of malignancy (Caron et al., *Cancer Res.* 1998, 58, 1930), osteopenia (Lark et al., *J Bone Miner. Res.* 2001, 16, 319), endometriosis (Healy et al., *Hum. Reproductive Update*, 1998, 4, 736), angiogenesis, including tumor angiogenesis (Cheresh, *Cancer Metastasis Rev.*, 1991, 10, 3-10 and Brooks et al., *Cell*, 1994, 79, 1157), retinopathy including macular degeneration (Friedlander et al., *Proc. Natl. Acad. Sci USA* 1996, 93, 9764), arthritis, including rheumatoid arthritis (Badger et al., *Arthritis Rheum.*, 2001, 44, 128), periodontal disease, psoriasis and smooth muscle cell migration (e.g. restenosis) and atherosclerosis (Brown et al., *Cardiovascular Res.*, 1994, 28, 1815)." Likewise, amended claim 13 provides a method for treating $\alpha_v\beta_5$ -mediated tumor metastasis, $\alpha_v\beta_5$ -mediated tumor growth and $\alpha_v\beta_5$ -mediated solid tumor growth. As described at page 2, lines 6 to 12 of the specification, "the integrin $\alpha_v\beta_5$ plays a role in neovascularization. Antagonists of the $\alpha_v\beta_5$ integrin will inhibit neovascularization and will be useful for treating and preventing angiogenesis, metastasis, tumor growth, macular degeneration and diabetic retinopathy." Accordingly, one of ordinary skill in the art of oncology would be able to practice the invention as claimed because the claims as amended are directed to $\alpha_v\beta_3$ -mediated conditions and $\alpha_v\beta_5$ -mediated conditions respectfully. As such, claims 11 and 13 are not so broad as to lack enablement under 35 U.S.C. §112, first paragraph.

Claim 10 is directed to a pharmaceutical composition. It is respectfully submitted that claim 10 is enabled by the description at pages 27-28 of the specification.

Claim 15 is directed to a method for treating neoplasia using a combination of the antagonists of the present invention with known chemotherapeutic agents. It is respectfully submitted that the standard treatment of various solid tumors using various chemotherapeutic

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agents is well known in the art. As such, the scope of the claim is not overly broad such that one skilled in the art would be able to combine the standards of treatment for a given neoplasia and the compounds of the present invention to practice the present invention.

Because the scope of the claims as amended is commensurate in scope with the teachings in the specification and the general knowledge available to one of ordinary skill in the art, it is respectfully submitted that claims 10, 11, 13 and 15 are sufficiently enabled under 35 U.S.C. §112, first paragraph. Reconsideration and withdrawal of the rejection is respectfully requested.

Previous Rejections under 35 U.S.C. §112, first paragraph

Applicants acknowledge the withdrawal of rejections labeled a), b), c) and e) of the previous office action.

D. Definitions of X

Claim 8 is amended to include X⁷ and X⁸ to overcome the rejection as described in the previous response filed October 8, 2003.

F. Definiteness of Claim 9

Claim 9 is amended to correct the open bracket and overcome the rejection.

G. Definiteness of Claims 10-16

Claims 10-16 are rejected for alleged indefiniteness as requiring undue experimentation to determine the scope of the claims. However, as described above with respect to the rejection under 35 U.S.C. §112, first paragraph, Applicants respectfully submit that amended claims 10, 11, 13 and 15 are sufficiently clear such that one skilled in the art would be able to practice the present invention. Accordingly, it is respectfully submitted that the claims satisfy the requirements of 35 U.S.C. §112, second paragraph.

H. Definiteness of Claim 15

Claim 15 is rejected because the term "chemotherapeutic agent" is indefinite. However, Applicants respectfully submit that the term "chemotherapeutic agent" is sufficiently clear to be

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understood by one of ordinary skill in the art. Breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). "If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. §112, second paragraph." MPEP 2173.04. Accordingly, claim 15 satisfies 35 U.S.C. §112, second paragraph.

I. Claim 16

Claim 16 has been canceled, thereby mooting the rejection.

Rejections under 35 U.S.C. §102

Applicants gratefully acknowledge withdrawal of the rejections under 35 U.S.C. §102.

New Rejections under 35 U.S.C. §112, first paragraph

A. Haloalky

Claim 8 has been amended to replace the term "haloalky" with "haloalkyl."

B. Z¹ on A-B ring

The depiction of Z¹ on the A-B ring has been amended to more clearly indicate that Z¹ is a divalent moiety. The depiction includes Z¹ to show its position relative to the A-B ring; however, Z¹ remains bonded to Z² as shown in Formula I.

C. R⁷⁹ and R⁸¹

The definitions of -OR substituents in the A1 moieties of claim 8 have been amended to overcome the rejection and to more clearly indicate that R (now designated as R⁸) may be H, alkyl or amino.

D. B and R⁴

Claim 8 has been amended to replace B and R4 with the correct designations of B⁴ and R⁷⁹ respectively.

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E. B4

The rejection is obviated by the correction of B⁴ and R⁷⁹ stated above.

Provisional Double Patenting Rejection

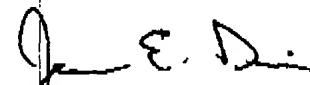
Claims 8-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of application serial number 10/363,070. Because no subject matter of either application has yet been found to be allowable, Applicants submit that this rejection is premature. Applicants will address the rejection to the extent necessary once the claims have been found to be otherwise allowable.

Conclusion

It is believed that the present application is in condition for allowance. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (314) 446-7683.

Applicants do not believe that any fee is required by the timely submission of this response. However, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 08-0750. Further, if there is any other fee deficiency or overpayment of any fees in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or credit such overpayment to Deposit Account No. 08-0750.

Respectfully submitted,

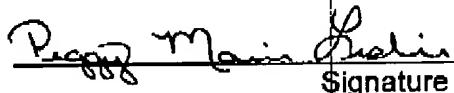


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Amendment B (12 pages)
Fax Cover Sheet (1 page)

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